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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/043,502	01/09/2002	David E. Burstein	2420/III29US2	9180

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EXAMINER

YU, MISOOK

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/043,502

Applicant(s)

BURSTEIN, DAVID E.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 8-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8/26/02.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group 1 encompassing claims 1-7 in the reply filed on 09/24/2004 is acknowledged. The traversal is on the ground(s) that claims 16-19 should be rejoined because claims 16-19 are directed to a method of distinguishing among epithelial tumors with or without squamous differentiation (or differential potential), therefore the search involves "p63 and squamous epithelial tumor" and the specific organ from which the tumor is derived such as lung or cervix should be irrelevant. This is not found persuasive because the search is not limited to "p63 and squamous epithelial tumor". The elected claims 1-7 are drawn to method of classifying a group of lung carcinomas into different subgroups using a biomarker, i.e. p63. However, group IV, claims 16-19 are not limited to method of classifying a group of lung carcinomas into different subgroups using the biomarker, rather group IV involves renal cancer classification using the biomarker. Searching of "p63 with squamous epithelial tumor" resulted in Ratovitski et al., (2000, Proc. Natl. Acad. Sci. USA., vol. 97, pages 5462-7), which discloses that p63 is expressed in lung squamous cell carcinoma, but reviewing Ratovitski et al., does not lead to conclude claims 16-19 are obvious or anticipated. Therefore, group IV invention involves different text searching both in the non-patent literature databases as well as patent database for the specifically claimed subtypes of carcinoma classification. This puts a serious burden on the examiner. The subject matter is carcinoma classification from different organs, which is not trivial.

Art Unit: 1642

subject matter in terms of evaluating the prior art, and examination. The requirement is still deemed proper and is therefore made FINAL.

Claims 8-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-24 are pending, and claims 1-7 are examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 uses "lung cancer, carcinoma" and "lung cancer carcinoma". It is not clear whether the two have different meanings or not in terms of the property boundary being sought. If not, then using one phrase would eliminate confusion.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

Art Unit: 1642

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is interpreted as drawn to method of distinguishing a differentiated squamous cell lung carcinoma from an undifferentiated lung carcinoma by detecting p63 expression in cells from a lung carcinoma. The specification at page 6 lines 14-23 teaches that “p63” exists in three isoforms from two different promoters. The specification at page 19-23 (Example 1) teach that several differentiated lung cancer cells express p63 detectable with the monoclonal anti-p63 4A4, which is reactive against a region common to both the full-length and the truncated forms of p63, while cells from small cell undifferentiated carcinoma do not express p63.

The course syllabus with the title “Pathology of Lung Cancer” downloaded on 12/9/04 from [url>>http://www.metrohelath.org/clinical/pathology/syllabus/carcinoma.asp](http://www.metrohelath.org/clinical/pathology/syllabus/carcinoma.asp) at page 4 teaches that epithelial tumors of lung are classified histologically classified into 8 groups. Wang et al., (2002, Hum. Pathol. Vol. 33, pages 921-926) at Table 1 at page 922 teach that not only a differentiated squamous cell lung carcinoma but

Art Unit: 1642

bronchioloalveolar carcinoma, adenocarcinoma, adenosquamous carcinoma, and large cell carcinoma also express p63. Wang et al., teach only thing for sure by detecting p63 in cells from a lung carcinoma is that the lung carcinoma is not small cell carcinoma, or carcinoid because those two do not express p63. The detection would not give information about whether the lung cancer is adenocarcinoma as compared to a differentiated squamous cell lung carcinoma. However, instant base claim 1 says that detecting p63 expression in cells from any "lung cancer carcinoma" indicate the lung carcinoma is a squamous cell lung cancer.

Further, the claims as currently construed say that detection of any one of the six different isoforms of p63 (3 from each of the two different promoters) leads to distinguish a differentiated squamous cell lung cancer carcinoma from an undifferentiated lung cancer carcinoma. However, both OMIM with #603273 (note page 1, first paragraph) downloaded on 12/10/2004 from [url>>www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov), and Wu et al., (2003, Cancer Research, vol. 63, pages 2351-7) at page 2351 teach that the three transactivation (TA) containing isoforms of p63, and the isoforms lacking the TA would have opposite functions. In other words, the three TA containing isoforms of p63 act as tumor suppressors like the wild-type p53 protein, while the isoforms lacking TA work as oncoproteins. These disclosures imply that a lung cancer might not overexpress the isoforms containing the TA domain. If it did, then the definition "tumor suppressor" becomes meaningless. What was detected in Example 1 of the instant specification might have been detection of the other three isoforms lacking TA domain, since the specific monoclonal antibody used has the binding epitope common to both.

Art Unit: 1642

The definition of "p63" at page 6, lines 14-23 clearly indicates that "p63" encompasses all six isoforms. The specification does not teach overexpression of all six isoforms occurs in a differentiated squamous cell lung carcinoma. Since the art teaches that TA containing isoforms are tumor suppressors, it is highly unlikely that those are overexpressed in a cancer. Most cancer appears to be developed because of loss of a tumor suppressor, not overexpression of it.

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

Conclusion

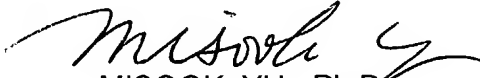
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

Art Unit: 1642

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


MISOOK YU, Ph.D.
Examiner
Art Unit 1642